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10/060,048	01/29/2002	Gregory Stephanopoulos	MTV-036.01	6568

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EXAMINER

MAHATAN, CHANNING

ART UNIT PAPER NUMBER

1631

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/060,048	<b>Applicant(s)</b> STEPHANOPOULOS ET AL.	
	<b>Examiner</b> Channing S. Mahatan	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2004.  
2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-35 and 46-48 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 1-35 and 46-48 is/are rejected.  
7) ☒ Claim(s) 1 and 12 is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### *APPLICANTS' ARGUMENTS*

Applicants' arguments, filed 15 October 2004, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### *CLAIMS UNDER EXAMINATION*

Claims herein under examination are claims 1-35 and 46-48.

### **Claims Rejected Under 35 U.S.C. § 101**

#### *NON-STATUTORY SUBJECT MATTER*

The rejection of claims 1-35 and 46-48 under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter is maintained for reasons of record. The claimed invention is directed to a "method for use in the analysis of gene or protein expression information"/"computer product for use in the analyzing gene or protein expression data"/"system".

Applicants submit the amendment to independent claims 1, 46, and 48 to include the step of using the measures of variability "in the analysis of gene or protein expression information" places the claims in compliance with 35 U.S.C. § 101. However, the amendments are found insufficient to overcome this rejection for the reasons below.

As previously indicated the instant claims appear to be "mental" processes of performing mathematical operations applied to a computer. Again, simply determining the variability of

Art Unit: 1631

expression levels provides no useful information; since there is no further indication (i.e. steps) of what the variability of expression levels represents. Applicants' amendment to merely use the measures of variability in analysis of gene or protein information does not provide any indication of what these measures are to represent. In such absence the claims do not recite any concrete or tangible results; therefore the claims do not recite statutory subject matter. Although a use is recited no additional steps for using the measures of variability in an analysis of gene or protein expression information is presented.

*USE CLAIM*

Claims 1, 46, 48, and all claims dependent therefrom are rejected under 35 U.S.C. § 101 because of the claimed recitation of "using the first measure of variability and the second measure of variability in an analysis of gene or protein expression information", without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. § 101. See for example *Ex parte Dunki*, 153 U.S.P.Q. 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 U.S.P.Q. 475 (D.D.C. 1966). The

**Claims Rejected Under 35 U.S.C. § 112 1<sup>st</sup> Paragraph**

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1631

*LACK OF ENABLEMENT*

The rejection of claims 1-35 and 46-48 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants submit the amendment to independent claims 1, 46, and 48 to include the step of using the measures of variability “in the analysis of gene or protein expression information” clearly expresses a “goal”. However, the amendments are found insufficient to overcome this rejection for the reasons below.

Claims 1-35 and 46-48 are rejected under 35 U.S.C. § 112, first paragraph. The instant claims fail to indicate the intended goal of using the measured variability “in the analysis of gene or protein expression information”. For example, in claim 1 what information is to be derived from said analysis by through the use of the measured variabilities? What is the final obtained result? Thus, in the absence of an intended goal that would be achieved through the implementation of the instantly claimed method, computer product, and system one skilled in the art would not understand what the information means and what to do with the information after the determination of measured variabilities (i.e. in the analysis of gene or protein information).

**Claims Rejected Under 35 U.S.C. § 112 2<sup>nd</sup> Paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1631

Claims 1-35 and 46-48 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

*VAGUE AND INDEFINITE*

Claims 1, 46, 48, and all claims dependent therefrom provides for “using the first measure of variability and the second measure of variability in an analysis of gene or protein expression information”, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process Applicants are intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. For instance, absent are the steps in the method of claim 1 for using the measured variabilities (i.e. first and second) in the analysis of gene or protein expression information. Clarification of the metes and bounds, via clearer claim language, is requested.

Claim 5, 6, and all claims dependent therefrom recite the limitation “wherein said comparison comprises determining a ratio” which is confusing (as amended). It is unclear what the ratio is. For instance, the instant claim 5 previously recited “the ratio of the measure of variability of (c) to the measure of variability of (b)”, wherein the (c) was understood to be the first measure and (b) was understood to be the second measure. Clarification of the metes and bounds, via clearer claim language, is requested.

Claim 35 and all claims dependent therefrom recite the limitation “wherein the F score may be calculated via transformation of a Wilks’ lambda score” which is considered vague and indefinite. The language “may be” implies an optional limitation, which further implies that

Art Unit: 1631

some criteria or parameter is to be applied such that it establishes whether or not these subsequent steps are to be performed (i.e. to calculate via a transformation of a Wilks' lambda score). Therefore, it is unclear if the subsequent are to be included in the method step or not. Clarification of the metes and bounds, via clearer claim language, is requested.

*LACK OF ANTECEDENT BASIS*

Claim 6 recites the limitation "wherein said comparison", however, no "comparison" are generated/derived in claim 1 and/or 2, which claim 6 depends from. Therefore, the above limitation lacks proper antecedent basis. Clarification of the metes and bounds, via clearer claim language, is requested.

**Claims Rejected Under 35 U.S.C. § 102**

The rejection of claims 1-6, 9-11, and 46-48 under 35 U.S.C. § 102(a) as being anticipated by Kerr et al. (Analysis of is maintained for reasons of record.

Applicants argue Kerr et al. does not: 1) separate samples into classes; and 2) teach all of the limitations of the rejected claims. However, Applicants argument is found unpersuasive for the reasons below.

Kerr et al. describes the analysis of variance for gene expression data taken from microarray (Title). The authors refer to such categories/classes (i.e. tissue type, strains of mice, or drug treatments) as varieties (instant claim 1 page 820, lines 7-13, page 821, lines 35-36, page 823, lines 3-5; and page 824, lines 22-26). It is noted the Applicants' disclosure states the following regarding classes representing different cellular states:

"Classes representing different cellular states may be defined by any relevant information about the sample." (page 65, lines 9-10)

Art Unit: 1631

Therefore, Kerr et al. teaches the classification of samples “into a number classes representing cellular states” claim limitation. Regarding the limitations of the rejected claims Applicants are to note specific citations to rejected claims were provided for in the prior ‘Non-Office Action’ mailed 13 July 2004 and is reiterated below. Kerr et al. describes the analysis of variance for gene expression data taken from microarray (Title). The authors indicate the method can be used to normalize microarray data and provide estimates of changes in gene expression that are corrected for potential confounding effects (instant claim 1; Abstract; page 820, lines 19-22). Kerr et al. determine the variances of the expression data, determines the differences in variances, determines the ratios of said differences, and scales said measures (instant claims 2-6 and 9; pages 820-824, beginning on line 24). Further, the authors indicate the calculation of variances may be performed to the  $g^{\text{th}}$  gene (i.e. wherein G is one or greater) (instant claims 10 and 11; page 820, lines 27-34). All computations for data analysis were carried out using Matlab software (instant claims 46-48 (i.e. computer product and processor); page 835, lines 26-28). Thus, Kerr et al. anticipates the instantly claimed invention.

#### *OBJECTION TO CLAIMS*

Claim 1 is objected to because of a grammatical error, wherein the instant claim has been amended to read “proteins in the for a number of samples”. Appropriate correction is requested.

Claim 12 is objected to because of a spelling error, wherein “protiens” should be replaced with “proteins”. Appropriate correction is required.



*ACTION IS FINAL AS NECESSITATED BY AMENDMENT*

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

*EXAMINER INFORMATION*

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either 571-273-8300.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S. Mahatan whose telephone number is (571) 272-0717. The Examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Art Unit: 1631

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Examiner Initials:

*CSM*

Date:

*March 16, 2005*

*Ardin H. Marschel 3/16/05*  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER